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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/171,671	05/01/2000	Martin Quibell	179-28	8322

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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/171,671	QUIBELL ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election on 7/28/2005 of the following species: septamers (it is believed that applicants intended heptamers i.e., seven-residue peptide) with the formula Abz-Val-Ala-Gln-Ser-Tyr(NO2)-Asn-NH2(Seq. ID. No. 24) including a FRET and a 96-well plate is acknowledged. Also, applicants' arguments on 12/16/2004 with respect to the examination of all of the present claims are also acknowledged.

Status of Claims

Claims 15-22 are pending and under examination.

Claims 1-14 have been cancelled.

Withdrawn Objection and Rejection:

In reply, in view of the submission of the new abstract, the objection to the specification is withdrawn. The 35 USC 112, second paragraph rejection in part has also been withdrawn. See further the rejection below. Also, the 35 USC 102(b)rejection over Deprez is withdrawn.

Specification

Response to Arguments

Applicants state that this application was filed under 35 U.S.C. 371 with a request to begin national examination and a copy of the International Application. This copy included substitute sheets which appear not to have been reviewed by the Examiner because the copy filed on October 23, 1998 does not refer to Table 11 (which appears on page 23) and does contain Figure 18 on sheet 17/17 of the drawings. The Examiner is requested to review the file and confirm that the copy of the application being examined is marked "SUBSTITUTE SHEET (RULE 26)" at the bottom of each page of the specification and drawings.

In response, the copy submitted under 35 USC 371 and reviewed by the examiner had the marked "***Substitute Sheets***" at the bottom of each page of the specification.

Upon review of the specification, there is Table 2 that refers to the different structural formula and Fig. 18. Accordingly, the objection to the disclosure is withdrawn.

It is requested that applicants submit a new, clear copy of the specification since the copy of the specification submitted under 35 USC 371 is ineligible as they are too blurry to read.

Information Disclosure Statement

The references submitted on 8/23/2004 have been considered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 15-22, newly added, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons advanced in the Office action of 3/23/2004.

Response to Arguments

Applicants state that all types of variations are not required to practice the claimed invention comprising of peptide of at least four residues B, C, D and E because there are b variants of amino acid B, c variants of amino acid C, d variants of amino acid D, and e variants of amino acid E. Insoluble peptides are excluded from the claimed invention: variations of the "two amino acid residues" selected from B, C, D or E (or the "other two amino acid residues") which result in a soluble

peptide comprise the mixtures making up the set of linear peptides in solution. Similarly, libraries not comprised of a peptide, which is an active substrate, or inhibitor of the enzyme is excluded from the claimed invention (i.e., there is "at least one" peptide which interacts with the enzyme). The amino acid sequences of peptides are indexed by their positions (or format) on plates of the L1 and L2 libraries. Certain features of the formatting of libraries which were disclosed in Applicants' specification have now been incorporated into the claimed invention: e.g., indexing of peptides by well position (or formatting) complies with the general deconvolution formulae recited in claim 15. The row and column positions of wells in a plate identify the amino acid sequence of the peptide which interacts with the enzyme. Applicants' experience has been that formatting libraries of linear peptides comprised of at least four amino acid residues in compliance with such formulae avoids the solubility and interaction phenomena cited by the Examiner in reference to Sharma. If this rejection is maintained, the Examiner is requested to provide evidence to support her assertion that libraries formatted in the manner described in claim 15 would suffer from the solubility and interaction phenomena discussed in the Office Action.

In response, the Office does not have the facilities and resources to provide the evidence needed in order to establish that by the format provided by the claims would result in a soluble peptide as claimed. It is incumbent upon applicants to provide the evidence, not by mere arguments or statements, in view of the evidence of record, the Sharma reference. Sharma discloses that a major limitation of the soluble library approach is its applicability to high affinity systems. The abundance of each compound in solution can be influenced by the total number of compounds in a library which can affect the biological activity. For this reason, a highly active compound in any pool may not in fact be the most potent molecule. Lack of reasonable solubilities of certain members in a library may further influence this phenomenon. In fact, for several libraries the most active peptide was not even identified in the most active library pool. The arguments that the formatting of the members in a library suffices solubility determination contradict the prior art wisdom. The genus claims do not have any amino acid residues for each or any member of the library to ascertain the claim to a soluble peptide that is simply based formatting of the peptides in the wells. There are too numerous unpredictable effects for amino acids interactions, even in a single well, that influence said solubility phenomenon. In this

respect attention is directed to the remarks made by applicants at page 6 of the 7/28/2005 REMARKS. Applicants state that the general combinatorial formula Aa-Bb-Cc-Dd-n(Ee)-Ff-Gg further includes G, a typically polar, invariant amino acid (e.g., Asp) that many libraries will also have to improve solubility. Thus, it appears from applicants' statement that solubility resides not in the formatting of the sequences on plates rather in the presence of amino acids in a peptide sequence in a library. The relevance of such formatting to the solubility of the peptide is also not apparent for the species recited at pages 55-60 of the specification. This section shows that no a priori prediction can be made even for a single heptamer species. It describes how the residues in the heptamer peptide, some cannot be measured, others do not show hydrolysis (synonymous to solubility?) and a handful produced a result. If applicants already encountered such unpredictable effect and difficulty in measuring or predicting which peptides from the specific ones would result in the object of the instant method, how much for a skilled artisan, given no specific guidance in the specification? There is no written description for the innumerable residues, singly or in combinations, artificial or natural, that fall within the scope of the claimed genus library of no defined structures. Blondelle, cited in the last Office action, states at page 2285

that even the presence of a protecting group in a soluble library can result in lack of activity of a peptide. A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials. University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See also University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Applicants, at the time of filing, are deemed to have not invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). In biotechnological invention one cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. [This is evident from applicants' disclosure, as stated above]. One may not preempt an unduly large field by the expedient of making broad prophetic statements in the specification and claim unless

the accuracy of such statements is sufficiently supported by well-established chemical principles or by sufficient number of examples.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-22, newly added, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons set forth in the last Office action.

Response to Arguments

In view of the amendments to the claims deleting the terms "adapted" and "active" the rejection with respect to these terms is withdrawn.

With respect to the term "unique", applicants state that as used in the claims is clear in its context. The autodeconvolution strategy disclosed in Applicants' specification requires "placing the mixtures of peptides separately each into individual wells positioned on plates" of the L1 and L2 libraries. Peptides in an individual well have

amino acid sequences with common residues at two positions (i.e., "all variations") and non-common residues at the other two positions (i.e., a unique pair). So uniqueness is characterized by the degree of variation at those positions.

In response, applicants' definition of uniqueness as to the degree of variation at certain positions makes it more confusing. It is not clear as to how the ***degree*** of variation is determined or measured.

Claim 15 is indefinite as to step (a). It is not clear as to how the L1 and L2 libraries are formed in such a way that any two peptides which are found together in one mixture of L1 is not found together in any one mixture of L2, especially in the absence of any structure for each of the residues.

Claim 22 is indefinite as this limitation is already contained in the base claim 15. The term "consist" especially when combined with the phrase "at least four" would read on claim 15 "comprising".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meldal (J.Chem. Soc. Perkin Trans.) in view of Deprez (J. Am. Chem. Soc.) and Pirrung et al (J. Am. Chem. Soc.)

Meldal discloses at pages 1591-1595, specifically the Experimental section, a method of screening for an enzyme by making a portion mixing library of substrates containing a Lys Abz at the C-end and nitrotyr at the N-end as an efficient donor-acceptor pair as FRET of the formula FQPLPLAVK. The library is then contacted with enzyme, substilisin to determine the substrates and inhibitors of the enzyme. Meldal does not teach a pair of (orthogonal)libraries and deconvolution formulae. However Deprez discloses at page 5405 a method of using orthogonal libraries i.e., use of a pair of libraries. The first library uses 25 amino acids partitioned into A1-A5. The second library uses the same 25 amino acids. Deprez states that the use of orthogonal self-deciphering libraries (auto-deconvolution, as claimed) offers several advantages, inter alia, it allows the screening of compounds in their soluble form. Pirrung discloses at e.g., page 1241, Fig. 1 a matrix for a combinatorial synthesis for indexing library. At page 1244,

Conclusion section, Pirrung provides the advantages of using this indexed or matrix library. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a two orthogonal library in a matrix format in the method of Meldal for the advantages taught by Deprez and Pirrung. The several advantages taught by Deprez (of autodeconvolution of two libraries) and Pirrung would provide the motivation to one having ordinary skill in the art. The claimed general deconvolution formulae would have been obvious to determine based on the orthogonal method taught by Deprez and matrix format (see formulae at page 1242) of Pirrung.

Applicants' arguments with respect to Deprez is moot in view of the new grounds of rejection, supra.

Double Patenting

Claims 15 and 20-22 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-6 of prior U.S. Patent No. 6,528,275 ('275 Patent). This is a double patenting rejection.

The instant claimed method is the same as the method of the '275 Patent which comprises the same components in the method. See applicants' statement at page 5 of the 7/28/2005 REMARKS with respect to the elected species as to "…..the allowability of the pending claims in light of US 6,528,275…). Also, as

interpreted in light of the specification, the instant disclosure and claimed method is drawn only to a 7-mer peptide which is the same as in the '275 Patent.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,528,275. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed method encompasses the '275 method which recites the specific 7-mer peptide.

The elected species is free of prior art. The examination of the pending claims had been extended to the generic claim as provided supra.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the

organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
October 15, 2005